REMARKS

Claims 1–15 were pending in this application prior to the amendment presented above. Claims 1 and 3–15 were withdrawn by the Examiner as directed toward non-elected inventions. Although Applicants disagree with the restriction of the claims, claims 1 and 3-15 have been cancelled without prejudice to the filing of a divisional application directed thereto. Claim 2 is amended herein to omit recitations directed to non-elected inventions, and new claims 16–18 have been added to provide a more complete claim set directed to the elected invention.

Support for the new claims is as follows. Claim 16 finds support at page 12 of the specification, lines 1 to 3, which describes the observation that upregulation of ERRα levels increases osteoblast differentiation. Further, at page 12, lines 22 to 24, it is indicated that disorders associated with bone loss or bone degeneration may be treated by promoting bone formation by increasing ERRα activity, for example by administration of an ERRα agonist, as noted at page 12, line 30. Claim 17 is supported at page 12, lines 18 to 21 of the specification, which lists disorders associated with bone loss or bone degeneration. Claim 18 is supported by page 16, lines 14 to 17 and by page 19, lines 15 to 18, of the specification.

Applicants submit that the new claims are supported by the application as originally filed, and respectfully request thereof.

The remaining issues raised by the Examiner in the Office Action are addressed below.

35 U.S.C. 112, first paragraph, enablement

The Examiner has rejected claim 2 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement.

As noted by the Examiner, claim 2 is directed to a method of increasing differentiation of osteoblasts in a mammal comprising administering to the mammal an effective amount of ERRα agonist. The Examiner further notes that the examples teach that inhibition of ERRα expression blocks the differentiation of rat calvaria cells to osteoblasts and that over-expression of ERRα increases differentiation and bone nodule formation of rat calvaria cells.

The Examiner argues that the specification teaches that ERRα is involved in osteoblast differentiation but fails to teach how ERRα is regulated or to correlate ERRα expression induced by estrogen, vitamin D3 or TGFβ with osteoblast differentiation.

Claim 2 is directed to a method of increasing osteoblast differentiation by administration of an ERRα agonist and not by an agent which effects ERRα expression. Applicants respectfully submit that the regulation of ERRα expression is not relevant to the claim under examination. Nevertheless, Applicants have shown a positive relationship between ERRα expression and osteoblast differentiation, and it is irrelevant whether Applicants have also demonstrated a correlation between estrogen, vitamin D3 or TGF β-induced ERRα expression and osteoblast differentiation.

The Examiner further argues that the term "ERRα agonist" can encompass a large genus of molecules, that the specification does not indicate a representative number of agonists and that therefore the specification fails to teach how to bring about increased osteoblast differentiation by administration of an ERRα agonist. The Examiner argues that undue experimentation would be required to use the claimed invention.

Firstly, the specification does teach methods for identifying an ERRα agonist.

At page 13 of the specification as filed, lines 11 to 13, the application teaches that agonists or antagonists of ERRα may be identified by screening for their effects in an assay for ERRα activity. ERRα activity may be measured, for example, by examining osteoblast differentiation in the cell systems described in the examples of the application, as noted at page 13, lines 20 to 24.

Additionally, other methods of identifying ERRα agonists are known to those of skill in the art. The enclosed journal articles, Suetsugi et al. "Flavone and Isoflavone Phytoestrogens are Agonists of Estrogen-Related Receptors" (2003), *Mol. Cancer Res.* **1**:981–991 (Tab A), and Zuercher et al. "Identification and Structure Activity Relationship of Phenolic Acyl Hydrazones as Selective Agonists for the Extrogen-Related Orphan Nuclear Receptors ERRβ and ERRγ" (2005) *J. Med.*

Chem. **48**:3107–3109 (Tab B), describe the identification of ERR agonists by methods known to those of skill in the art, showing that once one has been alerted by the teachings of the present application to the utility of ERRα agonists for promoting cartilage formation, one could, using known methods, identify suitable agonists using no more than routine skill.

In the Suetsugi et al. paper, at page 983, it is reported that three isoflavones and one flavone were shown to be agonists of ERRα in a HeLa cell system. This system is a well-established model system in which nuclear receptor agonism and activity are tested and it has been used in many studies of ERRα.

The Zuercher et al. paper describes screening of candidate compounds for their effect as agonists of ERRα, ERRβ and ERRγ. Although the specific compounds described were not agonists of ERRα, the paper clearly shows that known methods can be used readily by those of skill in the art to identify ERRα agonists. As noted at page 3108, left column, compounds were screened using a FRET assay published in 1998, and as noted at page 3109, left column, by a previously described cell-based reporter assay using an $(ERE)_3$-TATA-luc reporter.

In view of the foregoing, Applicants respectfully submit that one of skill in the art, using known methods, could identify ERRα agonists without undue experimentation and that claim 2 is enabled by the specification as filed. Accordingly, Applicants respectfully request that the enablement rejection be withdrawn.

35 U.S.C. 112, first paragraph, written description

Claim 2 stands rejected under 35 U.S.C., 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

The Examiner argues that the claimed method of increasing osteoblast differentiation is not described because the specification does not set forth specific ERRα agonists and the Applicants are not in possession of the recited process steps of claim 2. Applicants respectfully disagree. One skilled in the art would find that the

Applicants were in fact in possession of the claimed invention at the time of filing. As noted above, page 13 of the specification as filed teaches methods for screening and identifying candidate compounds for their activity as ERRα agonists. Applicants thus submit that it was well understood by those of skill in the art at the priority date that one could screen for agonists using a combination of methods, firstly a biological assay as described at page 13 of the specification and then a molecular-biochemical study to determine if an observed biological effect was due to agonism of ERRα. All of these are routine assays, well within the purview of the skilled worker and not involving undue experimentation, giving Applicants possession of the claimed invention.

In view of the foregoing, Applicants respectfully submit that the teachings of the specification as filed do indicate that the Applicants were in possession of the claimed invention. Applicants therefore respectfully request that the written description rejection be withdrawn.

Claim Objection

Claim 2 is objected to as encompassing non-elected inventions. Claim 2 has been suitably amended herein to exclude non-elected inventions.

Conclusion

The points and concerns raised by the Examiner in the outstanding Office Action having been addressed in full, it is respectfully submitted that this application is in condition for allowance. Should the Examiner have any remaining concerns, it is respectfully requested that the Examiner contact the undersigned attorney at (919) 845-1400 to expedite the prosecution of this application to allowance.

Respectfully submitted,

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Attachments:
Tab A
Tab B

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